

1
2 Claims:

3 1 The use of a composition of PKB, its analogues,
4 isoforms, inhibitors, activators and/or the functional
5 equivalents thereof, to regulate glycogen metabolism
6 and/or protein synthesis.

7
8 2 The use of a composition of PKB, its analogues,
9 isoforms, inhibitors, activators and/or the functional
10 equivalents thereof, for the manufacture of a
11 medicament to regulate glycogen metabolism and/or
12 protein synthesis.

13
14 3 The use as claimed in claim 1, to
15 combat disease states where glycogen metabolism and/or
16 protein synthesis exhibits abnormality.

17
18 4 The use as claimed in claim 1, to combat
19 diabetes.

20
21 5 The use as claimed in any preceding claim, to
22 combat cancer.

23
24 6 The use as claimed in claim 5, wherein the cancer
25 is breast, pancreatic or ovarian cancer.

26
27 7 The use as claimed in claim 1, wherein
28 the PKB is PKB α , β or γ , an analogue, isoform,
29 inhibitor, activator or a functional equivalent
30 thereof.

31
32 8 The use as claimed in claim 1, wherein
33 the PKB, its analogue, isoform, or functional
34 equivalent is modified at one or both of amino acids
35 308 and 473 by phosphorylation and/or mutation.
36

1 9 A composition of PKB, its analogues, isoforms,
2 inhibitors, activators and/or the functional
3 equivalents thereof.

4
5 10 A peptide having or including the amino acid
6 sequence Arg-Xaa-Arg-Yaa-Zaa-Ser/Thr-Hyd, where Xaa is
7 any amino acid, Yaa and Zaa are any amino acid, and Hyd
8 is a large hydrophobic residue, or a functional
9 equivalent of such a peptide.

10
11 11 A peptide as claimed in claim 10, wherein Hyd is
12 Phe or Leu, or a functional equivalent thereof.

13
14 12 A peptide as claimed in claim 10,
15 wherein Yaa or Zaa or both are an amino acid other than
16 glycine.

17
18 13 A peptide as claimed in claim 10, having the amino
19 acid sequence GRPRTSSFAEG, or a functional equivalent
20 thereof.

21
22 14 A method of identifying agents able to influence
23 the activity of GSK3, said method comprising:

- 24
25 a. exposing a test substance to a substrate of GSK3;
26 and
27 b. detecting whether said substrate has been
28 phosphorylated.

29
30 15 A method of identifying agents which influence the
31 activity of PKB, comprising:

- 32
33 a. exposing a test substance to a sample containing
34 PKB, to form a mixture;
35 b. exposing said mixture to a peptide as claimed in

36 claim 10; and

1 c. detecting whether (and, optionally, to what
2 extent) said peptide has been phosphorylated.
3

4 16 A method as claimed in claim 14, wherein the
5 extent of phosphorylation of the peptide is determined.
6

7 17 A method as claimed in claim 15, wherein the
8 phosphorylation state(s) of one or both of amino acids
9 308 and 473 on PKB is determined.

10
11 18 A method as claimed in claim 14,
12 wherein the test substance is an analogue, isoform-
13 inhibitor, or activator of PKB.
14

15 19 A method as claimed in claim 14,
16 wherein steps a or b (or both) are carried out in the
17 presence of divalent cations and ATP.
18

19 20 A method of treatment of the human or non-human
20 animal body, said method comprising administering PKB,
21 its analogues, inhibitors, stimulators or functional
22 equivalents thereof to said body.
23

24 21 A method as claimed in claim 20, to combat disease
25 states where glycogen metabolism and/or protein
26 synthesis exhibits abnormality.
27

28 22 A method as claimed in claim 20, to combat
29 diabetes.
30

31 23 A method as claimed in claim 20, to combat
32 cancer.
33

34 24. A method as claimed in claim 23, wherein the
35 cancer is breast, pancreatic or ovarian cancer.
36

1 25 A method as claimed in claims 20
2 wherein the PKB is PKB α , β or γ , an analogue, isoform,
3 inhibitor, activator or a functional equivalent
4 thereof.

5
6 26 An agent capable of influencing the activity of
7 PKB, its isoforms, analogues and/or functional
8 equivalents, by modifying amino acids 308 and/or 473 by
9 phosphorylation or mutation.

i0
i1 27 A method of determining the ability of a substance
i2 to affect the activity or activation of PKB, the method
i3 comprising exposing the substance to PKB and
i4 phosphatidyl inositol polyphosphate and determining the
i5 interaction between PKB and the phosphatidyl inositol
i6 polyphosphate.

i7
i8 28 A method of determining the ability of a substance
i9 to combat diabetes, cancer, or any disorder which
i0 involves irregularity of protein synthesis or glycogen
i1 metabolism, the method comprising exposing the
i2 substance to PKB and phosphatidyl inositol
i3 polyphosphate and determining the interaction between
i4 PKB and the phosphatidyl inositol polyphosphate.

i5
i6 29 A method as claimed in claim 27,
i7 wherein the interaction between PKB and the
i8 phosphatidyl inositol polyphosphate is measured by
i9 assessing the phosphorylation state of PKB.

i0
i1 30 A method as claimed in claim 29, wherein the
i2 phosphorylation state of PKB at T308 and/or S473 is
i3 assessed.

i4
i5 31 A method of identifying activators or inhibitors
i6 of GSK3 comprising exposing the substance to be tested

1 to GSK3 and determining the state of activation of
2 GSK3.

3
4 32 A method as claimed in claim 31 wherein the state
5 of activation of GSK3 is determined by assessing its
6 phosphorylation.

7
8 33 A method of determining the suitability of a test
9 substance for use in combatting diabetes, cancer, or
10 any disorder which involves irregularity of protein
11 synthesis or glycogen metabolism, the method comprising
12 exposing the substance to be tested to GSK3 and
13 determining the state of activation of GSK3.

14
15 34 A method for screening for inhibitors or
16 activators of enzymes that catalyse the phosphorylation
17 of PKB, the method comprising exposing the substance to
18 be tested to

19 - one or more enzymes upstream of PKB;
20 - PKB; and (optionally)
21 - nucleoside triphosphate
22 and determining whether (and optionally to what extent)
23 the PKB has been phosphorylated on T308 and/or S473.